PATENT COOPERATION TREATY

PCT

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BUNT-001-PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/BE2004/000172	International filing date *(day/month/year)* 02.12.2004	Priority date *(day/month/year)* 02.12.2003

International Patent Classification (IPC) or national classification and IPC
A61P25/24, A61K31/343, A61K31/4545, G01N33/48, A61K31/00, A61P25/00, A61P25/28, A61P25/22, A61P25/16

Applicant
B&B BEHEER NV

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 13 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 21 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30.09.2005	16.03.2006

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/BE2004/000172

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-211	as originally filed
Claims, Numbers	
1-78	filed with telefax on 30.09.2005
Drawings, Sheets	
1-15	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/BE2004/000172

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-78 (in part)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☒ the claims, or said claims Nos. 1-78 (in part) are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-78
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-78
Industrial applicability (IA)	Yes:	Claims	1-78
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item I

Basis of the report

1. The amendments filed with the International Bureau under Article 19(1) introduce subject-matter which extends beyond the content of the application as filed, contrary to Art. 19(2) PCT. The amendments concerned are the following:

   a) Claim 1: "...wherein said second compound is selected from the group comprising: ...acetylcholinesterase inhibitor... and tachykinin antagonist...". According to the application as originally filed (cf. description p. 34-167 and claims 47-76), combinations comprising the enumerated (second) compounds are used for the treatment of specific disorders and not for any of the diseases listed under (i)-(iv).

   b) Claims 24, 26-29: The application as originally filed does not seem to provide any basis for the term "... (eti)levodopa/decarboylase inhibitor ...".

   c) Claims 45-66: "... according to claim ... 43 ...". Claims 45-66 refer to Alzheimer, but not claim 43.

   d) Claim 76: The application as originally filed does not seem to provide any basis for item (c) "...measuring the selective affinity of a test compound to adrenergic receptors and histamine receptors...".

   The amended set of claims thus is not allowable under Art. 19(2) PCT.

   The following general remarks can however be made.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

2. Claims 1-78 are not supported by the description as required by Art. 6 PCT.
   The claims are directed to an extremely large number of possible diseases and "second" compounds. Nevertheless, the experimental protocol disclosed in the present application only refers to the combination treatment of major depression, OCD and panic disorders with pipamperone-citalopram. No alternatives are envisaged.

3. The doses defined in claims 1-78 lack clarity (Art. 6 PCT).

Re Item IV

Lack of unity of invention

4. a) The application lacks unity within the meaning of Rule 13.2 PCT.

-The problem to be solved in claims 1-24, 30-75 and 77-78 of the present application is the provision of a medicament for the treatment of diseases with an underlying dysregulation of the emotional functionality selected from (i) non-cognitive metal disorders, (II) cognitive diseases, (III) pain disorders, (iv) Parkinson disease.

The proposed solution is the use of pipamperone in combination with a second compound selected from the groups enumerated in claim 1.

-The problem to be solved in claims 25-29 is the provision of a medicament for the treatment of the underlying emotion dysregulation of Parkinson disease.

The proposed solution is the use of pipamperone in combination with a levodopa/decarboylase inhibitor compound (not mentioned in claim 1).

-The problem to be solved in claim 76 of the present application is the provision of a method for preparing a compound having a selective D4 and 5-HT2A antagonist, reverse agonist or partial agonist activity.

The corresponding method is described in claim 76.

Claims 1, 25 and 76 thus include within their scope problems and solutions which are clearly different.

The separate inventions do not seem too be linked so as to form a single general inventive concept.

It is pointed out that the use of compounds having a selective D4 and 5-HT2A antagonist, reverse agonist or partial agonist activity such as pipamperone in the treatment of diseases e.g. diseases with an underlying dysregulation of the emotional functionality such as Parkinson disease is already known to the skilled person (cf. amongst others D1-21).

b) Furthermore, the application lacks unity within the meaning of Rule 13.2 PCT for the following reasons.

The problem underlying claims 1-24, 30-75 and 77-78 of the present application is the provision of a medicament for the treatment of diseases with an underlying dysregulation of the emotional functionality selected from (i) non-cognitive metal disorders, (II) cognitive diseases, (III) pain disorders, (iv) Parkinson disease (cf. claim 1).

The proposed solution is the use of pipamperone in combination with a second

compound selected from the groups enumerated in claim 1.

Pipamperone has already been used in combination with several active agents falling within the definition of claim 1 for the treatment of diseases with an underlying dysregulation of the emotional functionality such as e.g. behavioural problems, depression, anxiety, dysthymia, psychotic disorders, bipolar disorders, mania etc (cf. amongst others D1-21).

The use of pipamperone in combination with a second compound selected from the groups cited in claim 1 can therefore not be considered as a linking technical feature between the diseases enumerated in claim 1, which all are distinct and have different causes and mechanisms, their treatments representing different technical problems with their own solutions.

There is thus no special technical feature linking the treatment of the aforementioned diseases.

Furthermore, since pipamperone has already been used in combination with several active agents falling within the definition of claim 1 for the treatment of diseases with an underlying dysregulation of the emotional functionality such as e.g. behavioural problems, depression etc, the treatment of diseases with an underlying dysregulation of the emotional functionality selected from those cited in claim 1 can no longer serve as a general inventive concept linking the different groups of combinations in claim 1, which have no other special technical feature in common.

Claim 1(-24, 30-75 and 77-78) thus includes within its scope distinct problems and distinct solutions which are clearly different.

The requirements of unity thus have not been met and there is no single inventive concept underlying the plurality of inventions.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

5. References:

D1: US-A-5 762 960 (DODMAN NICHOLAS H) 9 June 1998 (1998-06-09)

D2: VOLMAT R ET AL: "The treatment of depressions by Cledial. Evolution and clinical state and handwriting" PSYCHOLOGIE MEDICALE 1986 FRANCE, vol. 18, no. 10, 1986, pages 1615-1622, XP009028776

D3: SQUELART P ET AL: "Pipamperone (Dipiperon), a useful sedative neuroleptic drug in troublesome

chronic psychotic patients." ACTA PSYCHIATRICA BELGICA. BELGIUM 1977 MAR-APR, vol. 77, no. 2, March 1977 (1977-03), pages 284-293, XP009028314 ISSN: 0300-8967

D4: KOCH H J ET AL: "Successful therapy of tardive dyskinesia in a 71-year-old woman with a combination of tetrabenazine, olanzapine and tiapride." INTERNATIONAL JOURNAL OF CLINICAL PRACTICE. ENGLAND MAR 2003, vol. 57, no. 2, March 2003 (2003-03), pages 147-149, XP009030046 ISSN: 1368-5031

D5: DIEBOLD K. ET AL: "Are psychoactive-drug-induced changes in plasma lipid and lipoprotein levels of significance for clinical remission in psychiatric disorders?." PHARMACOPSYCHIATRY, (1998) 31/2 (60-67)., 1998, XP009029360

D6: WO 98/43646 A (BROEKKAMP CHRISTOPHORUS LOUIS ;PINDER ROGER MARTIN (NL); AKZO NOBE) 8 October 1998 (1998-10-08)

D7: PERUGI G ET AL: "EFFECTIVENESS OF ADJUNCTIVE GABAPENTIN IN RESISTANT BIPOLAR DISORDER: IS IT DUE TO ANXIOUS-ALCOHOL ABUSE COMORBIDITY?" JOURNAL OF CLINICAL PSYCHOPHARMACOLOGY, WILLIAMS AND WILKINS, US, vol. 22, no. 6, 2002, pages 584-591, XP009029358 ISSN: 0271-0749

D8: ADLER L ET AL: "PRAXIS DER STATIONAEREN AKUTBEHANDLUNG VON MANIEN RETROSPEKTIVE VERGLEICHSUNTERSUCHUNG AN JE 100 PATIENTEN ZWEIER PSYCHIATRISCHER ZENTREN PRACTICE OF IN-PATIENT ACUTE TREATMENT OF MANIAS" FORTSCHRITTE DER NEUROLOGIE PSYCHIATRIE, STUTTGART, DE, vol. 62, no. 12, 1994, pages 479-488, XP009029389 ISSN: 0720-4299

D9: ANSOMS C ET AL: "Sleep disorders in patients with severe mental depression: double-blind placebo-controlled evaluation of the value of pipamperone (Dipiperon)." ACTA PSYCHIATRICA SCANDINAVICA. FEB 1977, vol. 55, no. 2, February 1977 (1977-02), pages 116-122, XP009041169 ISSN: 0001-690X

D10: LEYSEN J E ET AL: "RECEPTOR INTERACTIONS OF NEW ANTIPSYCHOTICS: RELATION TO PHARMACODYNAMIC AND CLINICAL EFFECTS" INTERNATIONAL JOURNAL OF PSYCHIATRY IN CLINICAL PRACTICE, MARTIN DUNITZ, LONDON, GB, vol. 2, no. 1, 1998, pages S03-S17, XP001009585 ISSN: 1365-1501

D11: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1996, SCHOTTE A ET AL: "Risperidone compared with new and reference antipsychotic drugs: In vitro and in vivo receptor binding" XP002290498 Database accession no. PREV199698819913

D12: VANHOENACKER P ET AL: "EFFICIENT EXPRESSION OF THE HUMAN DOPAMINE D4.2 RECEPTOR: POSITIVE INFLUENCE OF PIPAMPERONE ON EXPRESSION LEVELS" ABSTRACTS OF THE SOCIETY FOR NEUROSCIENCE, SOCIETY FOR NEUROSCIENCE, WASHINGTON, DC, US, vol. 26, no. 1/2, 2000, page 1, XP001181469 ISSN: 0190-5295

D13: VIJVER VAN DE D A M C ET AL: "ANTIPSYCHOTICS AND PARKINSON'S DISEASE: ASSOCIATION WITH DISEASE AND DRUG CHOICE DURING THE FIRST 5 YEARS OF ANTIPARKINSONIAN DRUG TREATMENT" EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY, SPRINGER VERLAG, DE, vol. 58, no. 7, 2002, pages 157-161, XP009033980 ISSN: 0031-6970

D14: ENGELBORGHS S ET AL: "AMINO ACIDS AND BIOGENIC AMINES IN CEREBROSPINAL FLUID

OF PATIENTS WITH PARKINSON'S DISEASE" NEUROCHEMICAL RESEARCH, PLENUM PRESS, NEW YORK, US, vol. 28, no. 8, August 2003 (2003-08), pages 1145-1150, XP009031514 ISSN: 0364-3190

D15: DATABASE EMBASE [Online] ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL; 1999, ETCHEPAREBORDA M C: "Neurocognitive and pharmacological approach to specific learning disorders" XP002312308 Database accession no. EMB-2000050033

D16: WIRZ-JUSTICE A ET AL: "HALOPERIDOL DISRUPTS, CLOZAPINE REINSTATES THE CIRCADIAN REST-ACTIVITY CYCLE IN A PATIENT WITH EARLY-ONSET ALZHEIMER DISEASE" ALZHEIMER DISEASE AND ASSOCIATED DISORDERS, RAVEN PRESS, NEW YORK, NY, US, vol. 14, no. 4, 2000, pages 212-215, XP009029353 ISSN: 0893-0341

D17: FAHS H ET AL: "THYMOREGULATEURS DANS L'AGITATION ET LES TROUBLES DU COMPORTEMENT CHEZ LE SUJET DEMENT A PROPOS DE HUIT CAS ANTICONVULSIVANTS AND AGGRESSIVE BEHAVIORS IN ALZHEIMER'S DISEASE. EIGHT CASES REPORTS" ENCEPHALE, PARIS, FR, vol. 25, no. 2, 1999, pages 169-174, XP009039295 ISSN: 0013-7006

D18: GRÖZINGER M ET AL: "Melperone is an inhibitor of the CYP2D6 catalyzed O-demethylation of venlafaxine." PHARMACOPSYCHIATRY. GERMANY JAN 2003, vol. 36, no. 1, January 2003 (2003-01), pages 3-6, XP009029363 ISSN: 0176-3679

D19: WERTH ESTHER ET AL: "Decline in long-term circadian rest-activity cycle organization in a patient with dementia." JOURNAL OF GERIATRIC PSYCHIATRY AND NEUROLOGY. 2002 SPRING, vol. 15, no. 1, April 2002 (2002-04), pages 55-59, XP009042127 ISSN: 0891-9887

D20: DE 40 39 631 A (TROPONWERKE GMBH & CO KG) 17 June 1992 (1992-06-17)

D21: STAHL STEPHEN M ET AL: "Examination of nighttime sleep-related problems during double-blind, placebo-controlled trials of galantamine in patients with Alzheimer's disease." CURRENT MEDICAL RESEARCH AND OPINION. APR 2004, vol. 20, no. 4, April 2004 (2004-04), pages 517-524, XP009041652 ISSN: 0300-7995

6. The present application refers to the use of pipamperone in combination with a second therapeutic agent selected from the groups enumerated in claim 1, in the treatment of diseases or disorders with an underlying dysregulation of the emotional functionality selected from the groups cited in claim 1.
The present application does not meet the requirements of Art. 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Art. 33(2) PCT, in view of D1-21.

D1 discloses combination therapies for the treatment of animal **behavioural problems** wherein **pipamperone** reduces mental **anxiety** and **clomipramine** providing sedation for the animal.

In D2, a **depressive** patient with **anxiety** was administered **medifoxamine, chlorazepate, levomepromazine, flunitrazepam** and **pipamperone.**

In D3, chronic schizophrenic patients with **troublesome behaviour and/or dysthymia**, received a combination of incisive neuroleptics such as **flupenthixol, haloperidol, pipothiazine, thioproperazine, trifluperidol, penfluridol, fluphenazine decanoate, fluspirilene,** and **pipamperone.**

In D4, a patient with **depression,** headache and orofacial dyskinesia had been treated with **haloperidol, pipamperone, zopiclone, citalopram.**

D5 refers to a clinical study wherein **psychiatric patients with depressive or schizoaffective disorders** were administered butyrophenones e.g. butyrophenones such as **pipamperone** and tricyclics and **SSRIs,** e.g. **fluvoxamine** and lithium.

D6 discloses combination comprising **mirtazapine** and antipsychotic agent such as **pipamperone,** used for treating **psychotic disorders e.g. schizophrenia, mania, hyperactivity, substance abuse.**

D7 discloses the concurrent use of **gabapentin, carbamazepin** and **pipamperone** in the treatment of **bipolar disorders.**

D8 discloses the therapy of **manic patients** with a combination of the **neuroleptics haloperidol** and **pipamperone.**

D9 refers to the treatment of sleep disorders in **depressive** patients with **pipamperone** in combination with **imipramine, chlorimipramine or amitriptyline.**

D10-12 disclose the selective affinity of **pipamperone** for the **5-HT2A and D4 receptors.**

D13 discloses the treatment of **Parkinson disease** with agents such as **levodopa** and the concomitant use of antipsychotic agents such as **pipamperone** to counter the psychosis as a complication.

D14 describes the treatment of **Parkinson** patients with **pergolide and/or levodopa, or**

levodopa, selegiline and anticholinergic drugs. Parkinson patients suffering from further cognitive deterioration were further treated with **pipamperone**.

D15 discloses the use of **pipamperone** optionally in combination with **selegiline** in the treatment of **cognitive disorder.**

In D16 patients with early onset **Alzheimer Disease** received **pipamperone** in combination with **risperidone and citalopram**.

D17 discloses combinations of **pipamperone, meprobamate, moclobemide, carbamazepine** or **pipamperone, meprobamate, zuclopenthixol, alimemazine, hydroxyzine** as anticonvulsivants and against aggressive behaviors in **Alzheimer disease.**
D18 discloses combinations of **venlafaxine and pipamperone.**

D19 discloses combinations of **pipamperone and haloperidol** or **pipamperone, lorazepam and clomethiazol** in demented patients with probable **Alzheimer disease.**

D20 discloses combination preparations consisting of (A) an active ingredient with a serotonin agonistic effect, which has a bonding strength on 5-HT 1A receptors smaller than 10000 nmol/l such as **gepirone** and (B) an active ingredient with a serotonin antagonistic effect which has a bonding strength on 5-HT2 receptors smaller than 1000 nmol/l such as **pipamperone** used in neuroprotective pharmaceuticals esp. in the treatment of cerebral ischaemia.

D21 relates to sleep disorders in **Alzheimer Disease** patients treated with **galantamine.** Some patients were simultaneously treated with **dipiperon** as antipsychotic.

7. The same reasoning appears to apply, mutatis mutandis, to the subject-matter of the corresponding independent claims 25, 76.

8. Dependent claims 2-24, 26-75, 77-78 do not seem to contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, see documents D1-21 and the

corresponding passages cited in the search report.

9. The following observations regarding inventive step may be added (Art. 33(3) PCT).
The experimental protocol disclosed in the present application only refers to the combination treatment of major depression, OCD and panic disorders with pipamperone-citalopram. Further diseases and agents falling within the definition of claims 1-78 have not been tested.
There is no substantiated basis of an inventive step for any subject-matter extending beyond these embodiments (Art. 33(3) PCT).
Moreover, most of the "second compounds" cited in the present application are well-known in the field of activity at issue. Coadministration with said compounds does therefore not render the claimed subject-matter inventive.

Re Item VIII

Certain observations on the international application

10. According to the description "... the invention relates to the use of compounds, which have D4 and 5-HT2A antagonist, inverse agonist or partial agonist activity for the treatment of the underlying emotion dysregulation of mental disorders..." (cf. p. 4, l. 1-5). The compounds may be administered in a mono-therapeutic context (cf. p. 4, l. 28-30). These statements in the description imply that the subject-matter for which protection is sought may be different to that defined by the claims, i.e. the use of pipamperone in combination with a second therapeutic agent, thereby resulting in lack of clarity (Art. 6 PCT) when used to interpret them.

11. In view of the numerous claims and the few tests carried out, it is considered that the present application does not fulfill the requirements of conciseness in the sense of Art. 6 PCT and does not meet the criteria of Rule 6.1(a) PCT regarding the numbering of claims.

Claims (retyped)

1. Use of pipamperone for the preparation of a medicament for treating a disease or disorder with an underlying dysregulation of the emotional functionality, wherein said pipamperone is administered to a patient in a dose ranging between 5 and 15 mg of the active ingredient, and wherein a second compound is administered simultaneously with, separate from or sequential to said pipamperone to augment the therapeutic effect of said second compound,
wherein said diseases or disorders with an underlying dysregulation of the emotional functionality is selected from the group consisting of :
(i) non-cognitive mental disorders comprising mood disorders, anxiety disorders, psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, pervasive development disorders, attention-deficit disorders, disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational problems, identity problem, phase of life problem, academic problem and problems related to abuse or neglect;
(ii) cognitive diseases comprising delirium, Alzheimer Disease, substance-related persisting dementia, vascular dementia, dementia due to HIV disease, dementia due to head trauma, dementia due to Parkinson Disease, dementia due to Huntington Disease, dementia due to Pick Disease, dementia due to Creutzfeldt-Jacob Disease, amnestic disorders due to a general medical condition, substance-induced persisting amnestic disorder, mild cognitive impairment disorder, other cognitive disorders;
(iii) pain disorders; and
(iv) Parkinson Disease; and
wherein said second compound is selected from the group comprising:
5-HT reuptake enhancer, 5-HT1 autoreceptor agonist, 5HT1A receptor agonist, 5-HT1A receptor antagonist, 5-HT1B receptor antagonist, 5-HT2B receptor antagonist, 5-HT2C receptor antagonist, 5-HT3 receptor antagonist, 5-HT6 receptor antagonist, adrenergic transmitter releaser, α1 adrenoreceptor antagonist, α2 adrenoreceptor antagonist, β3 adrenoreceptor agonist, cannabioid receptor antagonist, D1 receptor agonist, D2 receptor antagonist, D3 receptor antagonist, DA uptake inhibitor, dopamine receptor agonist, H3 receptor antagonist, compounds which increase brain concentrations of 5-HT, levodopa, MAO reuptake inhibitor, MAO-A & MAO-B reuptake inhibitor, MAO-B inhibitor, MAO-B re-uptake inhibitor, NARI, NaSSA, NDRI, RIMA, SDA, SDRI, Second messenger beta agonist, SNDRI, SNRI, SSRI; acetylcholinesterase inhibitor, AMPA receptor mediator compound, amyloid aggregation-inhibitor compound, calcium channel modulator, choline uptake enhancer, ERK activator, GABA agonist, histamine H3-receptor antagonist, compounds which increase insulin sensitivity, compounds which mimic the effect of NGF, muscarinic receptor partial agonist, NGF gene therapy, nicotinic receptor agonist compound, NMDA antagonist compound, non-steroidal anti-inflammatory drug (NSAID) PDE4 inhibitor compound, peptidic compound, compounds which protect dopaminergic and cholinergic neurons, CRF1 antagonist, GR antagonist, MT receptor agonist, neurotensin receptor antagonist, NK2 receptor antagonist, NK3 receptor antagonist, substance P receptor (NK1) antagonist compound; and, tachykinin antagonist.

2. Use according to claim 1, wherein said pipamperone is administered daily at least one day before administering said second compound.

3. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases or disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, substance related disorder, personality disorders, antisocial behaviour, bereavement, occupational problem and problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT (serotonin) reuptake enhancer compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT (serotonin) reuptake enhancer compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

4. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases or disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, substance related disorder, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT1 autoreceptor agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT1 autoreceptor agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

5. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender disorders, sleep disorders, adjustment disorders, impulse control disorders, attention-deficit disorders, substance-related disorder, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT1A (serotonin 1A) receptor agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT1A (serotonin) 1A receptor agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

6. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender disorders, adjustment disorders, impulse control disorders, substance-related disorder, personality disorders, antisocial behaviour, bereavement, occupational problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT1A receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT1A receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

7. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorder, personality disorders, antisocial behaviour, bereavement, occupational problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT1B receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT1B receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

8. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorder, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT2B receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT2B receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

9. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating

disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorder, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT2C receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT2C receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

10. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of substance-related disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT3 receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT3 receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

11. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a cognitive disorder selected from the group of diseases and disorders consisting of Alzheimer Disease, substance-induced persisting dementia, vascular dementia, dementia due to HIV disease, dementia due to head trauma, dementia due to Parkinson Disease, dementia due to Huntington Disease, dementia due to Pick Disease, dementia due to Creutzfeldt-Jacob Disease, amnestic disorders due to a general medical condition, substance-induced persisting amnestic disorder, mild cognitive impairment disorder and other cognitive disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT6 receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT6 receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

12. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, adjustment disorders, impulse control disorders, personality disorders, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of an adrenergic transmitter releaser compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said adrenergic transmitter releaser

compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

13. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, personality disorders, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a alpha 1 adrenoreceptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said alpha 1 adrenoreceptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

14. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, substance related disorders, personality disorders, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a alpha 2 adrenoreceptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said alpha 2 adrenoreceptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

15. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse ~~control dis~~orders, substance related disorders, personality disorders, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a beta 3 adrenoreceptor agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said beta 3 adrenoreceptor agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

16. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion

dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting mood disorders, anxiety disorders, psychotic disorders, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, pervasive development disorders, disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational problem, identity problem and problems related to abuse or neglect, pain disorders and delirium, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a cannabioid receptor 1 antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said cannabioid receptor 1 antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

17. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of substance related disorders and Parkinson disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a D1 receptor receptor agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said D1 receptor receptor agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

18. Use of pipamperone or a pharmaceutically acceptable salt thereofaccording to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting mood disorders, psychotic disorders, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, pervasive development disorders, disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational problem, identity problem and problems related to abuse or neglect, pain disorders and delirium, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a D2 receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said D2 receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

19. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of psychotic disorders, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, pervasive development disorders, disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational problem, identity problem, problems related to abuse or

neglect, pain disorders and delirium, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a D3 receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said D3 receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

20. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of substance related disorders and Parkinson disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a DA (dopamine) uptake inhibitor compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said DA (dopamine) uptake inhibitor compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

21. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, adjustment disorders, impulse control disorders, attention-deficit disorders, substance-related disorders, personality disorders and problems related to abuse or neglect, pain disorder and Parkinson disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a dopamine receptor agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said dopamine receptor agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

22. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a cognitive mental disease or disorder selected from the group of diseases and disorders consisting of Alzheimer Disease, substance-induced persisting dementia, vascular dementia, dementia due to HIV disease, dementia due to head trauma, dementia due to Parkinson Disease, dementia due to Huntington Disease, dementia due to Pick Disease, dementia due to Creutzfeldt-Jacob Disease, amnestic disorders due to a general medical condition, substance-induced persisting amnestic disorder, mild cognitive impairment disorder and other cognitive disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a histamine H3 receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said histamine H3 receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

23. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion

dysregulation of a non cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorders, personality disorders, bereavement, occupational problem, problems related to abuse or neglect and pain disorder, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a compound which increases brain concentrations of 5-HT (serotonin) to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said compound which increases brain concentrations of 5-HT (serotonin), further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

24. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of Parkinson Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of an (eti)levodopa/decarboylase inhibitor compound, possibly in combination with entacapone, to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said levodopa/decarboylase inhibitor compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

25. A pharmaceutical composition comprising (a) pipamperon, and (b) a levodopa/decarboylase inhibitor compound, preferably is (eti)levodopa/carbidopa, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof possibly in combination with entacapone, which is an inhibitor of catechol-O-methyltransferase (COMT), or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof, as a combined preparation for simultaneous, separate or sequential use for treating the underlying emotion dysregulation of Parkinson Disease.

26. A pharmaceutical composition according to claim 25, wherein pipamperone is provided in a unitary dose of between 5 and 15 mg of the active ingredient and wherein said (eti)levodopa/decarboylase inhibitor compound is levodopa / carbidopa, preferably provided in a unitary dose of between 250 to 600 mg and 25 to 150 mg of the active ingredients.

27. A pharmaceutical composition according to claim 25, wherein pipamperone is provided in a unitary dose of between 5 and 15 mg of the active ingredient and wherein said (eti)levodopa/decarboylase inhibitor compound is levodopa / benserazide, preferably provided in a unitary dose of between 100 to 600 mg and 25 to 150 mg of the active ingredients.

28. A pharmaceutical composition according to claim 25, wherein pipamperone is provided in a unitary dose of between 5 and 15 mg of the active ingredient and wherein said (eti)levodopa/decarboylase inhibitor compound is levodopa / benserazide.

29. A pharmaceutical composition according to any of claims 25 or 26, wherein pipamperone is provided in a unitary dose of between 5 and 15 mg of the active

ingredient and wherein said (eti)levodopa/decarboylase inhibitor compound is levodopa / carbidopa or etilevodopa / carbidopa in combination with entacapone, of which the latter is preferably provided in a unitary dose of between 500 mg and 100 mg of the active ingredient.

30. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of non-cognitive mental disease or disorder which are substance related disorders and Parkinson disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a monoamine oxidase (MAO) reuptake inhibitor compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said monoamine oxidase (MAO) reuptake inhibitor compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

31. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, adjustment disorders, impulse control disorders, attention-deficit disorders, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorder, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a monoamine oxidase A (MAO-A) and a monoamine oxidase B (MAO-B) reuptake inhibitor compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said monoamine oxidase A (MAO-A) and a monoamine oxidase B (MAO-B) reuptake inhibitor compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

32. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, adjustment disorders, impulse control disorders, attention-deficit disorders, substance-related disorders, personality disorders, problems related to abuse or neglect, pain disorder and Parkinson disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a monoamine oxidase B (MAO-B) inhibitor compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said monoamine oxidase B (MAO-B) inhibitor compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

33. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of Parkinson Disease, characterized in that pipamperone or said

pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a monoamine oxidase B (MAO-B) reuptake inhibitor to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said monoamine oxidase B (MAO-B) reuptake inhibitor, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

34. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, adjustment disorders, attention-deficit disorders, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorder, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a selective nor-adrenaline re-uptake inhibitor (NARI) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said selective nor-adrenaline re-uptake inhibitor (NARI) compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

35. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a noradrenergic/specific serotonergic antidepressant (NaSSA) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said noradrenergic/specific serotonergic antidepressant (NaSSA) compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

36. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, adjustment disorders, attention-deficit disorders, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a selective nor-adrenaline and dopamine re-uptake inhibitor (NDRI) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said selective nor-adrenaline and dopamine re-uptake inhibitor (NDRI) compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

378. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, adjustment disorders, impulse control disorders, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a compound which is a reversible inhibitor of mono-amine oxydase A (RIMA) to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said compound which is a reversible inhibitor of mono-amine oxydase A (RIMA), further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

38. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, psychotic disorders, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, pervasive development disorders, disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational problem, identity problem, problems related to abuse or neglect, pain disorder and delirium, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a serotonin/dopamine antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said serotonin/dopamine antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

39. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorders, personality disorders, antisocial behaviour, bereavement, occupational ~~problem~~, problems related to abuse or neglect, pain disorders, delirium, Alzheimer Disease, substance-induced persisting dementia, vascular dementia, dementia due to HIV disease, dementia due to head trauma, dementia due to Parkinson Disease, ~~dementia due to~~ Huntington Disease, dementia due to Pick Disease, dementia due to Creutzfeldt-Jacob Disease, amnestic disorders due to a general medical condition, substance-induced persisting amnestic disorder, mild cognitive impairment disorder and other cognitive disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a selective serotonin and dopamine re-uptake inhibitor (SDRI) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said selective serotonin and

dopamine re-uptake inhibitor (SDRI) compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

40. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, personality disorders, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a second messenger beta agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said second messenger beta agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

41. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, attention-deficit disorders, substance-related disorders, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a selective serotonin, nor-adrenaline and dopamine re-uptake inhibitor (SNDRI) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said selective serotonin, nor-adrenaline and dopamine re-uptake inhibitor (SNDRI) compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

42. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, attention-deficit disorders, substance-related disorders, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a selective serotonin and nor-adrenaline re-uptake inhibitor (SNRI) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said selective serotonin and nor-adrenaline re-uptake inhibitor (SNRI) compound, further characterized in that

pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

43. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorders, personality disorders, antisocial behaviour, bereavement, occupational problem, problems related to abuse or neglect and pain disorders, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a selective serotonin re-uptake inhibitor (SSRI) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said selective serotonin re-uptake inhibitor (SSRI) compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

44. Use according to claim 1 or 2, wherein said disease or disorder is Alzheimer disease.

45. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a 5-HT6 antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said 5-HT6 antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

46. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of an acetylcholinesterase inhibitor compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said acetylcholinesterase inhibitor compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

47. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of an AMPA receptor mediator compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said AMPA receptor mediator compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

48. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of an amyloid aggregation-inhibitor compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said amyloid aggregation-inhibitor compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

49. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a calcium channel modulator compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said calcium channel modulator compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

50. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a choline uptake enhancer compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said choline uptake enhancer compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

51. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a compound that activates ERK (extracellular signal-related kinase) to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said compound that activates ERK (extracellular signal-related kinase), further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

52. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a GABA agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said GABA agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

53. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion

dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a histamine H3-receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said histamine H3-receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

54. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a compound which increases insulin sensitivity to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said compound which increases insulin sensitivity, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

55. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a compound which mimics the effect of nerve growth factor (NGF) to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said compound which mimics the effect of nerve growth factor (NGF), further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

56. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a muscarinic receptor partial agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said muscarinic receptor partial agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

57. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a selective nor-adrenaline and dopamine re-uptake inhibitor (NDRI) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said selective nor-adrenaline and dopamine re-uptake inhibitor (NDRI) compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

58. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion

dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to nerve growth factor (NGF) gene therapy, to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said nerve growth factor (NGF) gene therapy, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

59. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a nicotinic receptor agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said nicotinic receptor agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

60. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of an N-Methyl-D-aspartate (NMDA) antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said N-Methyl-D-aspartate (NMDA) antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

61. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a non-steroidal anti-inflammatory drug to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said a non-steroidal anti-inflammatory drug, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

62. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a phosphodiesterase-4 (PDE4) inhibitor compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said phosphodiesterase-4 (PDE4) inhibitor compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

63. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate

from or prior to the administration of a peptidic compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said peptidic compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

64. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a compound which protects dopaminergic and cholinergic neurons to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said compound which protects dopaminergic and cholinergic neurons, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

65. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a selective serotonin and dopamine reuptake inhibitor (SDRI) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said selective serotonin and dopamine reuptake inhibitor (SDRI) compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

66. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1, 2 or 43, for the preparation of a medicament for treating the underlying emotion dysregulation of Alzheimer Disease, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a selective serotonin, nor-adrenaline and dopamine re-uptake inhibitor (SNDRI) compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said selective serotonin, nor-adrenaline and dopamine re-uptake inhibitor (SNDRI) compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

67. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive_mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, ~~somatoform~~ disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, substance related disorders, personality disorders, bereavement, occupational problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a CRF1 antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said CRF1 antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

68. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorders, personality disorders, bereavement, occupational problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a GR antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said GR antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

69. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorders, personality disorders, bereavement, occupational problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a melatonin receptor (MT) agonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said melatonin receptor (MT) agonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

70. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, psychotic disorders, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, pervasive development disorders, disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational problem, identity problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a neurotensin receptor antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said neurotensin receptor antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

71. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of

diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorders, personality disorders, bereavement, occupational problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a neurokinin 2 receptor (NK2) antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said neurokinin 2 receptor (NK2) antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

72. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, psychotic disorders, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sleep disorders, adjustment disorders, impulse control disorders, pervasive development disorders, disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational problem, identity problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a neurokinin 3 receptor (NK3) antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said neurokinin 3 receptor (NK3) antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

73. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, personality disorders, bereavement, occupational problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a peptidic compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said peptidic compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

74. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep

disorders, adjustment disorders, impulse control disorders, substance-related disorders, personality disorders, bereavement, occupational problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a substance P receptor (NK1) antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said substance P receptor (NK1) antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

75. Use of pipamperone or a pharmaceutically acceptable salt thereof according to claim 1 or 2, for the preparation of a medicament for treating the underlying emotion dysregulation of a non-cognitive mental disease or disorder selected from the group of diseases and disorders consisting of mood disorders, anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders (excluding pain disorders), factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, impulse control disorders, substance-related disorders, personality disorders, bereavement, occupational problem and problems related to abuse or neglect, characterized in that pipamperone or said pharmaceutically acceptable salt thereof is administered simultaneously with, separate from or prior to the administration of a tachykinin antagonist compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said tachykinin antagonist compound, further characterized in that pipamperone is to be administered to a patient in a daily dose ranging between 5 and 15 mg of the active ingredient.

76. A method for preparing a compound having a selective D4 and 5-HT2A antagonist, reverse agonist or partial agonist activity comprising the following steps:

(a) measuring the selective affinity of a test compound to the D4 receptor and selecting a compound that has a pKi value equal to or greater than 8 towards the D4 receptor in respect to all the other Dopamine receptors, and measuring the selective efficacy of the selected compound to the D4 receptor and selecting a compounds which is a selective antagonist, inverse agonist or partial agonist of the D4 receptor;

(b) measuring the selective affinity of a test compound to the 5-HT2A receptor and selecting a compound that has a pKi value equal to or greater than 8 towards the 5-HT2A receptor in respect to all the other 5HT receptors, and measuring the selective efficacy of the selected compound to the 5-HT2A receptor and selecting a compounds which is a selective antagonist, inverse agonist or partial agonist of the 5-HT2A receptor;

(c) measuring the selective affinity of a test compound to adrenergic receptors and histamine receptors, and selecting a compound that has a pKi value lower than 8 towards said adrenergic receptors and said histamine receptors, and measuring the selective efficacy of the selected compound to said adrenergic receptors and said histamine receptors, and selecting a compound which is not a selective antagonist, inverse agonist or partial agonist of said adrenergic receptors and said histamine receptors;

(d) identifying a compound which is selected in (a), (b), and (c), and

(e) preparing the compound identified in (d).

77. Use according to any of claims 1, 2 or 5, wherein said second compound is chosen from the group consisting of fluvoxamine controlled release, phenserine tartrate,

atomoxetine hydrochloride, bupropion (controlled-release formulation), ropinirole HCL (controlled-release formulation), INN 00835, galantamine (extended release formulation), paliperidone, tomoxetine, aprepitant, rivastigmine tartrate, ORG 34517/34850, sunepitron, sumanirole, milnacipran, idazoxan, xaliproden, SR 58611, befloxatone, litoxetine, tianeptine, agomelatine, SPD 503, flesinoxan, bifeprunox, ramelteon, etilevodopa, rasagiline (TVP-1012) and desvenlafaxine.

78. Use according to any of claims 1, 2 or 5, wherein said second compound is chosen from the group consisting of galantamine (extended release formulation), R121919, risperidone, paliperidone and R228060 (YKP-10A).